hydrochloride given alone and with steroids.[5] He had one ulcerative, exudative lesion 4 cm in diameter located on the nose (figure (*c*)).

Parasites isolated from the lesions of both patients were cultivated on blood agar medium and identified, by serological examination and isoenzyme analysis using thin layer starch gel electrophoresis, as *L tropica* of serotype $A_2$, the aetiological agent of recurrent cutaneous leishmaniasis.

In case 1 the parasites were eliminated from the lesions on the nose and upper portion of the cheek after 45 days of treatment but were still present in the lesion on the lower portion of the cheek. Another 20 days' treatment improved the lesion clinically, and an additional 20 days' treatment were required to eliminate the parasites totally. Healing was complete within three to four weeks after the end of treatment, with negligible scar formation on one lesion and good cosmetic results on the two others (figure (*b*)). The patient was observed for 12 months after the completion of treatment, during which time no relapse or any symptom of the disease occurred. The lesions were completely healed, and biopsy specimens were free of parasites.

During the first seven days of treatment in case 2 the lesion improved clinically but living parasites were still present. The patient was treated for an additional 73 days, after which time the parasites were completely eliminated and the lesion healed (figure (*d*)).

The treatment was well tolerated, and no adverse clinical or laboratory side effects occurred.

## Comment

Although the present study covered only 10-12 months of observation this treatment appears to be superior to the other available regimens because it is simple and does not cause discomfort or side effects.

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# Nutritional support improves antibody response to influenza virus vaccine in the elderly

Recent studies have confirmed that protein-energy malnutrition and deficiencies of several nutrients result in impaired immune responses, particularly cell mediated immunity.[1] In old age there is a progressive decline in immunological vigour,[2] and old people also show alterations in dietary intake, catabolism, and needs, with consequent changes in nutritional state and body composition. Many people over 65 have obvious or subclinical nutritional deficiencies.[3] We have observed that correction of nutritional deficits and imbalances may reverse, in part, the impairment of cell mediated immunity in the elderly.[4]

Respiratory infections are a common cause of illness in old age[5] and may be life threatening. Immunisation against influenza virus is frequently administered in an attempt to reduce morbidity due to this infectious agent. Very little is known, however, about the immunological response to these vaccines in elderly people who have nutritional deficiencies. We therefore report how improved nutritional intake enhances antibody response to influenza virus vaccine in old age.

## Subjects, methods, and results

During an epidemiological survey of the nutritional state of 100 elderly men, 30 aged 70-84 years were found who had abnormalities in at least two tests of clinical, biochemical (albumin, prealbumin, zinc concentrations), anthropometric (weight for height, skinfold thickness), and haematological (haemoglobin, ferritin values) fitness. Detailed nutritional data will be reported elsewhere. All the subjects lived independently in their own homes and none showed evidence of any acute or chronic serious systemic disease.

Each subject was inoculated with about $10^5$ $TCID_{50}$ (median tissue culture infective dose) influenza A/Hong Kong/77 (H1N1). Serum samples for determination of antibody titres were obtained before immunisation and 28 days after inoculation. Serum haemagglutination inhibition antibodies were assayed by the use of chicken red blood cells and purified H1N1 influenza A antigen. A titre of $< 1/4$ before immunisation was considered seronegative and a fourfold or greater rise of antibody titre taken as evidence of seroconversion.

The 30 subjects were allocated at random to two groups. For four weeks beginning on the day of vaccination one group received nutritional advice and oral dietary and medicinal supplements appropriate for the type of malnutrition documented in each case. The second group of 15 served as non-supplemented controls. There was no significant difference between the groups in nutritional state, age distribution, socioeconomic state, housing, or other demographic features.

Dietary advice and supplements resulted in an improvement in nutritional state. At the end of four weeks changes in weight (58·7 (SD 6·1) *v* 63·9 (5·5) kg), skinfold thickness (11·0 (SD 2·7) *v* 14·8 (1·8) mm), and serum prealbumin concentration (230 (SD 40) *v* 460 (70) mg/l) were statistically significant. There was a trend towards improved values in other anthropometric, haematological, and biochemical tests as well. Moreover, there were fewer subjects showing abnormally low values.

*Response to influenza virus vaccination in nutritionally supplemented elderly and non-supplemented controls*

| Group | No studied | No achieving seroconversion | Log reciprocal geometric mean antibody titre (SD) |
|---|---|---|---|
| Supplemented | 15 | 14* | 5·7 (1·2)† |
| Non-supplemented | 15 | 9 | 2·5 (0·7) |

*Compared with controls: $p < 0.05$ ($\chi^2$ test corrected for continuity).
†Compared with controls: $p < 0.01$ (paired Student's *t* test).

Antibody response to influenza virus vaccination was significantly better in the supplemented group (table), as shown by a higher rate of seroconversion and a higher mean antibody titre.

## Comment

The elderly make up a progressively growing segment of the population. A main health problem in old age is an increased incidence of infections, including respiratory illness.[5] In part, this may be the result of a progressive decline of immune function,[2] including depressed cell mediated immunity, decreased natural killer cell and phagocyte activity, and impaired epithelial barrier function.

Influenza virus infection is a common cause of serious respiratory illness in the elderly and may threaten survival. Hence vaccination is commonly given to this high risk group. Little is known, however, of the possible effect of frequently associated nutritional deficiencies on the immune response to the vaccine and the extent of protection achieved. In this study we observed a significantly increased rate of seroconversion and higher serum antibody titres in elderly men given nutritional supplementation for four weeks. Probably this improved immune response also confers better protection against influenza disease. It remains to be established, however, whether nutritional rehabilitation of elderly people *before* immunisation would have even greater beneficial effects in terms of both immune response as well as protection.

Nutritional deficiency is common in the elderly, and cell mediated immunity and other mechanisms of host resistance decline with aging. Since nutritional state is a critical determinant of immunocompetence, the correction of obvious or latent undernutrition in the elderly may be expected to improve immune responses, including that to vaccination against respiratory infections, and perhaps result in better protective immunity.

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# Fast atrial fibrillation induced by treatment of psoriasis with azathioprine

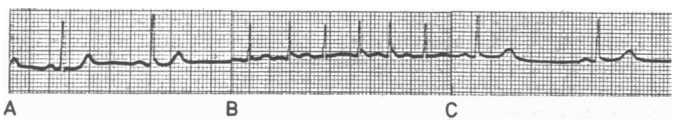
We describe a patient with psoriasis who developed fast atrial fibrillation in an idiosyncratic reaction to azathioprine.

## Case report

A 60 year old man was referred for treatment of widespread psoriasis. He had suffered from the condition for over 20 years and had received various topical treatments and photochemotherapy. The response to psoralens and ultraviolet A treatment had been unsatisfactory after some initial improvement, and immediately before his referral to our department he had been using potent topical steroid ointments. He had a history of heavy alcohol consumption. Examination showed widespread confluent plaques of psoriasis, which had a glazed, thinned appearance. No abnormal cardiovascular signs were found, and he was in sinus rhythm at 60 beats/min with a blood pressure of 140/90 mm Hg. An electrocardiogram on admission (figure (*A*)) and chest *x* ray film were normal. We considered him to be unsuitable for routine treatment with dithranol, and azathioprine 50 mg three times daily was started. He received no other drug.

Four days later he became febrile, and over the next 48 hours his temperature reached 40°C and was accompanied by a sinus tachycardia. Azathioprine was stopped, and repeated cultures of blood and urine yielded negative results. Three days later, after the fever and tachycardia had completely settled, azathioprine was reintroduced. Within five hours he developed rigors and a fever (39°C) and was found to be in fast atrial fibrillation (figure (*B*)). Azathioprine was again immediately stopped, and the atrial fibrillation resolved within hours on bed rest. Tests of thyroid function yielded normal results, and serum electrolyte concentrations and a later electrocardiogram (figure (*C*)) were normal.

Subsequent inquiries about previous treatment at another hospital showed that he had developed a fever while taking azathioprine seven years before. It had recurred on reintroduction of the drug.




Electrocardiogram (lead II) (*A*) on admission; (*B*) five hours after azathioprine 50 mg; and (*C*) after bed rest and withdrawal of azathioprine.

## Comment

Azathioprine is a widely used immunosuppressive agent that is effective in severe and disabling psoriasis.[1] Toxic effects include depression of bone marrow, hepatotoxicity, gastrointestinal upsets, reduced resistance to infection, malignant tumours, and teratogenicity. Because patients show better tolerance of and clinical response to methotrexate azathioprine has become a second line agent in severe psoriasis that is used when other treatments have failed or are contraindicated.[1]

Febrile reactions to azathioprine have been reported and can, as in our case, develop within hours after administration of the drug. The mechanism is unclear, but the fever may be associated with polyarthritis. We have found no reports of cardiac side effects of azathioprine, and neither the manufacturers (Wellcome Medical Division, United Kingdom) nor the Committee on Safety of Medicines has received reports of any such side effects in toxic reactions. Episodes of atrial fibrillation in normal hearts can be precipitated by other drugs, including alcohol,[2] inappropriate thyroxine treatment,[3] and nicotine,[4] as well as by non-cardiac events such as surgery, pneumonia, burns, mediastinal carcinoma, lymphoma, pulmonary embolism, and renal and biliary colic.[5] There was no precipitating event in our patient other than the administration of azathioprine, and the heart was clinically and electrocardiographically normal before and after the episode.

It is important for physicians using azathioprine to be aware of this serious but reversible adverse effect.

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# Orchidopexy: theory and practice

Only 32% of orchidopexies are done by the recommended age of 5 years. The number of operations is four times greater than the incidence of undescended testis, suggesting that boys with retractile testes have unnecessary surgery. We decided to investigate further.

## Present survey and results

With the help of colleagues in 12 hospitals in different parts of Britain we recorded the ages of 1285 boys undergoing orchidopexy between 1981 and 1983. The proportions who had surgery before the age of 5 ranged from 7% to 51%, with a mean of 32%.

We took the incidence of undescended testis as 1% and calculated the expected number of cases for six district hospitals with known catchment populations. In these the numbers of orchidopexies were two to four times greater than expected (table).

All general practitioners in the Medway district were asked when they would refer boys with undescended testis for surgery; of the 92 who replied, 69 (75%) said that they would do so before the age of 5 years.

We examined the hospital and, wherever possible, neonatal and community child health records of 58 boys who had had orchidopexies in 1983. In 15 cases the diagnosis had been made at the neonatal examination but none of these children, if otherwise well, had been followed up by paediatricians. In 22 cases the referral letter stated that the diagnosis had been made by a community medical officer, but in many cases the separate neonatal, hospital, child health clinic, and school medical records made it impossible to elicit this information.

Among these cases we found two where the testes had been noted to be

*Expected and actual numbers of orchidopexies performed in six district general hospitals*

| Hospital | No of male births a year | No of orchidopexies a year | |
|---|---|---|---|
| | | Expected | Performed |
| 1 (Medway) | 2500 | 25 | 52 |
| 2 | 1000 | 10 | 22 |
| 3 | 1900 | 19 | 43 |
| 4 | 1800 | 18 | 65 |
| 5 | 2000 | 20 | 87 |
| 6 | 1400 | 14 | 62 |
| England and Wales, 1981 | 315 000 | 3150 | 14 070 |